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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,843	12/02/2003	Hans Kurt Pingel	6207.520 -US	3225

23650 7590 03/09/2007

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,843	PINGEL ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8-15 and 17-24* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1652.

Applicant's response, on December 20, 2006, to the First Action on the Merits of this case mailed August 9, 2006, is acknowledged. It is acknowledged that applicants have cancelled Claims 7 and 16 and amended Claims 1-6 and 8-15. Claims 1-6, 8-15, and 17-24 are pending. Claims 17-24 were previously withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Claims 1-6 and 8-15 are hereby considered.

Priority

Applicants have requested that the present claims be accorded the benefit of DK PA 2000 01456, filed October 2, 2000. In support of said request, Applicants argue that DK PA 2000 01456 discloses culturing of Factor VII-producing cells in large-scale, according to the current claims. This argument is not found to be persuasive. It is acknowledged that Example 1 of DK PA 2000 01456 discloses large-scale culturing of Factor VII-producing cells in medium lacking serum. However, DK PA 2000 01456 fails to disclose large-scale culturing of Factor VII-producing cells in medium lacking animal-derived components, as recited in the instant claims. Therefore, the priority date granted for the elected invention is October 2, 2001, the filing date of US 09/969,357, which discloses large-scale production of a Factor VII polypeptide using medium lacking animal-derived components (pg 24).

Information Disclosure Statement-Objections

Applicants have requested clarification of the Examiners comments stating that parts of the Information Disclosure Statement filed December 2, 2003 fails to comply with 37 CFR 1.98(a)(1). As explanation, the following is provided. Specifically, the textual list of references found on page 2 of said Information Disclosure Statement fails to comply because said references are not presented on a 1449 form. As previously explained, page 2 of said Information Disclosure Statement has been placed in the application file, but the information referred to on said page has not been considered. If Applicants wish for the references therein to be considered, a supplemental Information Disclosure Statement should be submitted. Any subsequent rejection, based on consideration of the supplemental Information Disclosure Statement, will not be considered to be a new grounds for rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

> The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
> A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
> Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim not is patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been

obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Claims 1-6, 8-11, and 15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-3, 5, 8, 10-13, and 15-17 of US Application 10/394,086. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-6, 8-11, and 15 herein and Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08 are both directed to methods for large-scale production of Factor VII in medium lacking animal-derived components. The claims differ in that Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08 specifically recite methods wherein the culture is at least 100 liters. The portion of the specification in 10/394,08 that supports the recited methods includes embodiments that would anticipate Claims 1-6, 8-11, and 15 herein, e.g., methods for large-scale production of Factor VII in medium lacking animal-derived components, which are also the methods recited in Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08. Claims 1-6, 8-11, and 15 herein cannot be considered patentably distinct over Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08 when there are specifically recited embodiments (methods for large-scale production of Factor VII in medium lacking animal-derived components) that would anticipate Claims 1-6, 8-11, and 15 herein. Alternatively, Claims 1-6, 8-11, and 15 herein cannot be considered patentably distinct over Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08 when there are specifically disclosed embodiments in 10/394,08 that supports Claims 1-3, 5, 8, 10-13, and 15-17 of that application and falls within the scope of Claims 1-6, 8-11, and 15 herein, because it would have been obvious to a skilled artisan to modify the methods of Claims 1-3, 5, 8, 10-13, and 15-17 of

10/394,08 by selecting a specifically disclosed embodiment that supports those claims, i.e., methods for large-scale production of Factor VII in medium lacking animal-derived components, as disclosed in 10/394,08. One having ordinary skill in the art would have been motivated to do this, because such an embodiment, is disclosed as being a preferred embodiment within Claims 1-3, 5, 8, 10-13, and 15-17 of 10/394,08.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Rejection of Claim 10 under 35 U.S.C. 112, second paragraph, as being indefinite because, as explained in the prior action, the phrase "the cell-containing carriers" lacks antecedent basis, is maintained. The skilled artisan would not know the metes and bounds of the recited invention.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement/ Written Description

Rejection of Claims 1-6 and 8-15 under 35 U.S.C. 112, first paragraph lack of enablement and written description, for the reasons explained in the prior action, is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) The present invention is not directed to Factor VII-related polypeptides, but to methods of producing Factor VII and related polypeptides by culturing mammalian cells expressing said polypeptides in the absence of animal-derived components.

(B) Reference to Factor VII-related polypeptides has been deleted.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that the instant invention is directed to methods of making Factor VII. However, methods for making a particular product must define what the product is, i.e. the structure and function. The specification provides the following definitions.

> "As used herein, "Factor VII" or "Factor VII polypeptide" encompasses wild-type Factor VII, as well as variants of Factor VII exhibiting substantially the same or improved biological activity relative to wild-type Factor VII." (pg 6, parg 2)

As explained in the prior action, the specification does not reasonably provide enablement for large-scale production of any Factor VII polypeptide because the specification fails to establish the desired structure and function of all polypeptides produced by the recited method or a rational and predictable scheme for producing any polypeptide having the desired biological. Clearly, without defining the product, the skilled artisan is not enabled to use the recited method make any said product. In addition, the invention has not been described in such a way as to reasonably convey that the Inventors, at the time the application was filed, had possession of the claimed method for making any said product.

(B) Reply: It is acknowledged that reference to Factor VII-related polypeptides has been deleted from most claims; Claim 15 continues to refer to Factor VII-related polypeptides

(line 7). Moreover, as explained in (A) above, the specification fails to provide enablement for large-scale production of any Factor VII polypeptide because the specification fails to define the structure or properties of all said Factor VII polypeptides.

For these reasons and those presented in the prior action, rejection of Claims 1-6 and 8-15 under 35 U.S.C. 112, first paragraph, is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Rejection of Claims 1, 2, 5, 6, 15, and 16 under 35 U.S.C. 103(a) as being unpatentable over the Ragni et al, 2001 in view of Schmidtchen et al, 1998, for the reasons explained in the prior action, is maintained.

Rejection of Claim 3 under 35 U.S.C. 103(a) as being unpatentable over the combination of Ragni et al and Schmidtchen et al in view of Weikert et al, 1999, for the reasons explained in the prior action, is maintained.

Rejection of Claims 4 and 9-14 under 35 U.S.C. 103(a) as being unpatentable over the combination of Ragni et al and Schmidtchen et al in view of Chen et al, 1998, for the reasons explained in the prior action, is maintained.

Rejection of Claim 8 under 35 U.S.C. 103(a) as being unpatentable over the combination of Ragni et al and Schmidtchen et al in view of Reiter et al, 1990, for the reasons explained in the prior action, is maintained.

In support of their request that said rejections be withdrawn, Applicants provide the following arguments.

(C) Ragni et al is not prior art because DK PA 2000 01456, which predates Ragni et al, discloses the instant invention.

(D) Nothing in Ragni et al, Schmidtchen et al, or the combination thereof provide any expectation of success in large-scale production of Factor VII under serum-free conditions. Results obtained for recombinant expression of one protein cannot be extrapolated to other proteins; especially with respect to glycosylation patterns. In fact, Ragni et al discuss numerous challenges that could prevent large-scale production of clotting factors in serum-free cultures, such as stability (which is provided by serum proteins) and immunogenicity (an unpredictable property affected by culture conditions). Schmidtchen et al only disclose small-scale production of a non-Factor VII protein in serum-free medium; there is no expectation of success for large-scale production. Protein structure and function are unpredictably sensitive to culture conditions used for recombinant production.

These arguments are not found to be persuasive for the following reasons.

(C) Reply: Because DK PA 2000 01456 does not disclose the instant invention, Ragni et al is prior art; see the explanation above regarding the priority date for the instant invention.

(D) Reply: It is acknowledged that Ragni et al discuss the need for improvement in the production of recombinant clotting factors, especially the problems of stability and immunogenicity (pg 31). However, the instant claims fail to recite the limitations of structural or function stability or immunogenicity for the Factor VII proteins produced by the methods of the elected invention. Moreover, Ragni et al also state that third-generation methods for making

recombinant factors include the use of protein-free culture conditions (Abstract, col 2), providing an expectation of success for the methods rendered obvious by the combination of Ragni et al and Schmidtchen et al.

For these reasons and those provided in the prior actions, the above rejections under 35 U.S.C. 103(a) are maintained.

Applicant's amendment necessitated any new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Regarding filing an Appeal, Applicants are referred to the Official Gazette Notice published July 12, 2005 describing the Pre-Appeal Brief Review Program.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants'

remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sheridan Lee Swope, Ph.D.
Art Unit 1652

SHERIDAN SWOPE, PH.D.
PRIMARY EXAMINER